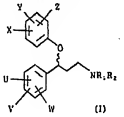
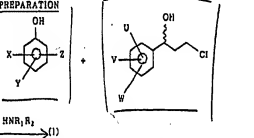
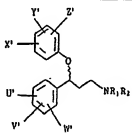


<p>92-398487/48 UNIV PENNSYLVANIA BOS UYPE- 91.05.01 *WO 9219210-A2 91.05.01 91US-694346 (92.11.12) A61K Novel serotonin re-uptake inhibitor cpds. - are antidepressants, also useful for imaging serotonin receptors when conig. radioactive holoen isotopes (Eng) CPL-176712 N(CA, 3P) R/AT BE CH DEK ES FR GB GR IT UG MC NL SE; Addnl. Date: KUNG H F 92.04.22 92WO-US03261</p>	<p>B(5-A3A, 5-A3B, 5-B1B, 7-H, 10-A4, 10-A8, 10-A10, 10-A13D, 10-A15, 10-A18, 10-A19, 10-B1A, 10-B7B, 11-C7B5, 12-C10, 12-G1, 12-K4A5) U, V, W, X, Y, Z = H, halo or 1-4C alkyl or 1-4C alkoxy (both opt. substid. by halo and/or OH); 1-6C heterocycle, 1-4C thioalkyl, NR<sub>2</sub>R<sub>1</sub>; -R<sub>1</sub>-A-R<sub>1</sub>; -A-R<sub>1</sub>; CN, SO<sub>2</sub>R<sub>2</sub>, NHCONH<sub>2</sub> or CONR<sub>2</sub>R<sub>1</sub>; R<sub>1</sub>, R<sub>2</sub> = H or 1-4C alkyl; R<sub>3</sub>, R<sub>4</sub> = 1-6C alkyl; R<sub>5</sub> = H, 1-6C alkyl, 1-6C heterocycle or -A-R<sub>1</sub>; R<sub>6</sub> = 1-4C alkyl or NR<sub>2</sub>R<sub>1</sub>; A = S, NH or O; provided that at least one of U-Z = halo.</p>
<p>Substd. 3-phenoxy-3-phenylpropylene derivs. of formula (I) and their salts are new:</p>  <p>(I)</p>	<p>Intermediate cpds. of formula (II) (see "Preparation") are also new.</p> <p>USE (1) bind to neurotransmitter reuptake sites and esp. inhibit serotonin reuptake. Radioactive halogen (esp. <sup>125</sup>I) labelled cpds. of (I) are useful for imaging serotonin receptors using single photon emission tomography (SPECT) to assess and improve treatment of psychiatric disorders. (I) may also be useful for in vitro binding studies and as therapeutic agents.</p> <p>WO9219210-A*</p>

<p><b>SPECIFICALLY CLAIMED</b> N-methyl-3-phenyl-3-(4-iodo-2-methylphenoxy)propylamine (1a),</p> <p><b>PREPARATION</b></p>  <p>Radioactive 1-labelled cpds. of (I) are prep'd. by treating the corresp. Br-cpd. with Et<sub>3</sub>N/tetrakis(triphenylphosphine) palladium, then stirring the resulting tributyltin deriv. (IIa) with I<sub>2</sub>/CHCl<sub>3</sub> or NaI/H<sub>2</sub>O, aq.).</p> <p>Other intermediates within the scope of (II) may be used to prepare the radiolabelled cpds. in an analogous manner.</p>	 <p>(II)</p> <p>one of U', V', W', X', Y', Z' = Sn(R<sub>1</sub>), Si(R<sub>1</sub>) or HgR and the others are as defined for U-Z; R = 1-5C alkyl.</p> <p><b>EXAMPLE</b> A mixt. of (R)-(+)-1-chloro-3-phenyl-3-(4-iodo-2-methylphenoxy)propane (0.58 g), eq. NaOH<sub>2</sub> (40%, 4 ml)</p> <p>WO9219210-A*/1</p>
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<p>92-398487/48</p> <p>and EtOH (1.5 ml) was heated at 130°C for 3 hr. in a sealed tube and worked up to give 0.25 g (44%) (R)-(-)-(1a) <math>\alpha^D_{20} = +11.98</math> (c 3.32, CHCl<sub>3</sub>); HCl salt had m.pt. 68°C, <math>\alpha^D_{20} = -8.34</math> (c 0.82, CHCl<sub>3</sub>).</p> <p>In in vitro competitive binding assays using rat brain tissue prepns. (1a). HCl had Ki 5 nM (serotonin uptake, [<sup>3</sup>H]-peroxetins) and IC<sub>50</sub> 20 nM (noradrenaline uptake, [<sup>3</sup>H]-nisoxetine), (26pp218AFDwgNo0/3).</p> <p>SR:No-SR:Pub</p>	<p>WO9219210-A/2</p>
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